IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Nagy Adly Habib, et al.	
Serial No:	10/625,232	
Filed:	July 22, 2003	Group Art Unit: 3739
Title:	APPLICATOR FOR MICROWAVE RADIATION TREATMENT	Examiner: Aaron F. Roane
Docket No:	22413-14	

DECLARATION UNDER 37 C.F.R. §1.132

I, Professor Henri Bismuth, M.D., declare and state as follows:

1. I am a doctor of medicine and Director of the Henri Bismuth Hepatobiliary Institute in Paris; Emeritus Professor of Surgery at the Faculty of Medecine Kremlin Bicêtre, Paris South University; and Honorary Consultant at the HepatoBiliary Center-Hôpital Paul Brousse-APHP, Paris. My specialties and areas of expertise are bile duct and liver surgery. My curriculum vitae is attached herewith.

2. I have reviewed U.S. Patent No. 5,472,441 to Edwards et al.; U.S. 5,836,906 to Edwards; U.S. 6,267,760 to Swanson; U.S. Patent Application No. 10/625,232; and an Office Action from the United States Patent and Trademark Office dated June 12, 2007. It is my understanding that independent claims 1 and 3 have been rejected on the basis that it would have been obvious to one of ordinary skill in the art to modify the invention of Edwards '441 as taught by Edwards '906 and Swanson '760 to achieve the invention claimed in claims 1 and 9. I disagree and I am of the opinion that it would not have been obvious from the teachings of Edwards et al. '441 in view of Edwards '906 and further in view of Swanson '760 to arrive at the invention claimed by claims 1 and 3 of the '232 application for the following reasons.

3. Resection is the total or partial removal of an organ. For individuals diagnosed with liver or kidney cancer, resection offers the best chance for cure or long-term survival. However, intraoperative blood loss has been identified as one of the major mortality predictors for liver and kidney surgery. Different strategies have been used in the past to minimize blood loss during resection. Indeed, the office action states that it is known to reduce bleeding and/or blood loss by heating tissue. The Applicant himself discloses that it is known that raising the temperature of body tissue tends to reduce blood flow within the tissue. With this I agree. I do not agree, however, that given this as background knowledge and given the teachings of Edwards '441; Edwards '906; and Swanson '760 it would have been obvious to develop the inventive method of claims 1 and 3.

4. The method claimed in claims 1 and 3 of U.S. Patent Application No. 10/625,232 uses the novel and unobvious method of heat coagulative necrosis in healthy tissue at a resection plane by the three-dimensional application of energy to achieve a bloodless resection. Due to the very nature of the claimed invention, most patients can have a liver or kidney resection performed without requiring a blood transfusion. Further, due to the bloodless nature of the resection no sutures or clips are necessary, it minimizes operative risk, lessens operating room time and patient stays at the hospital, and therefore results in a overall decrease in cost to the health care system.

5. As stated in paragraph 3, using electromagnetic ablation in the treatment of malignancies in not a new concept. However, resection of a portion of an organ such as liver to treat a malignancy must be contrasted with the mere ablation of a tumour as described by Edwards '441 et al. Ablation has been a widely recognized modality of treatment albeit with well-defined limitations. Ablation, in the original sense and as disclosed by the Edwards '441 et al. reference, is used to pierce a tumour with a sharp probe and apply thermal energy to eliminate active tumourous tissue. The probe is inserted through healthy tissue in order to reach the depth of the tumour. Electromagnetic energy is applied to the tumour and it is ablated. The healthy surrounding tissue is spared by the use of a retractable, insulative sheath. In other words, the three-dimensional application of heat to a volume of tissue is not taught or suggested by Edwards '441 et al. Rather, the pin point application to a localized site it taught by Edwards '441 et al.

6. Swanson '760 teaches the application of electromagnetic energy applied to a site of tissue by use of an applicator without needles. The surgeon then incises the tissue to the depth of application. The process is then repeated at the same site until the surgeon cuts through the tissue. It must be noted that the application of energy is again done in linear fashion. If an entire cancerous lobe of tissue must be excised the process must be repeated painstakingly along a planned incision line. If the foregoing surgical method were performed along a planned incision line using the device of Swanson '906 it would result in the uneven application of energy to the tissue and a bloodless resection that maintains a clean border of healthy tissue would not be possible.

7. The Examiner suggests that combining Edwards '441 with Swanson '760, i.e. to use needles in the Swanson '760 device, would be obvious and result in the method being claimed in claims 1 and 3. I disagree. The references do not suggest the three-dimensional application of energy in a volume of tissue to achieve a completely uniform heating pattern that allows tissue to be excised while maintaining a border of healthy tissue. This is a critical difference in the various methods and even more critical given the complex and highly vascularized nature of the liver.

8. The liver is highly vascularized and blood flow to, through and from the liver is complex. The splenic vein, joins the inferior mesenteric vein, which then together join with the superior mesenteric vein to form the hepatic portal vein, bringing venous blood from the spleen, pancreas, stomach, small intestine, and large intestine. The hepatic veins drain directly into the inferior vena cava. Approximately 60% to 80% of the blood flow to the liver is from the portal venous system. The hepatic artery, which accounts for 40% to 20% of the blood flow to the liver, is generally a branch from the celiac trunk, although occasionally some or all of the blood can be from other branches such as the superior mesenteric artery. The hepatic artery proper (also proper hepatic artery), arises from the common hepatic artery and joins the portal vein and the common bile duct to form the portal triad. It subsequently gives off the cystic artery which feeds the gallbladder before bifurcating into the right and left hepatic arteries. The hepatic artery not only distributes blood to the liver, but also to the pancreas and gallbladder as well as to the stomach and duodenal portion of the small intestine.

9. The central area where the common bile duct, hepatic portal vein, and hepatic artery enter the liver is the hilum or "porta hepatis." The duct, vein, and artery divide into left and right branches, and the portions of the liver supplied by these branches constitute the functional left and right lobes. The functional lobes are separated by a plane joining the gallbladder fossa to the inferior vena cava. This separates the liver into the true right and left lobes. The middle hepatic vein also demarcates the true right and left lobes. The right lobe is further divided into an anterior and posterior segment by the right hepatic vein. The left lobe is divided into the medial and lateral segments by the left hepatic vein. The fissure for the ligamentum teres (the ligamentum teres becomes the falciform ligament) also separates the medial and lateral segments. The medial segment is what used to be called the quadrate lobe. In the widely used Couinaud or "French" system, the functional lobes are further divided into a total of eight subsegments based on a transverse plane through the bifurcation of the main portal vein. The caudate lobe is a separate structure which receives blood flow from both the right- and left-sided vascular branches.

10. Thus although the precise techniques used in performing resections differ based on surgeons' preferences, the underlying principle remains the same: one must interrupt the flow of blood to the portion of liver being resected and due to the highly vascularized nature of the liver as described in paragraphs 7 and 8 above, this is not an easy task. Prior to the invention claimed by claims 1 and 3 of the '232 application, stapling devices, bioglues, haemostatic powders and the like were used without complete success. In other words, while the flow of blood was partially interrupted a bloodless resection was not possible. If a hypothetical device were created using the combination of Edwards '441, Swanson '760 and Edwards '906 it is my opinion that a bloodless resection would not be possible due to the uneven application of energy and the failure to deliver a consistent three-dimensional pattern of energy. By "bloodless resection" I mean that the device dramatically reduces the blood loss such that there is no need for a blood transfusion of any kind. Further, the device and method of the hypothetical combination would not be effective in a liver resection as it would be incapable of closing the size of vessels present in the liver necessary for a bloodless resection.

11. Furthermore, tumours in the liver tend to form in clusters making the removal of a single tumour impractible. Rather, the removal or resection of an entire portion of the liver is necessary. This is accomplished by identifying the outer boundary of the tumourous clusters with radiological imaging or intra-operative ultrasound techniques. The outer boundary of the cluster formation constitutes healthy tissue. Thus the method claimed in claims 1 and 3 uses a device that is inserted along a planned incision line of healthy tissue in stepwise fashion and electromagnetic energy applied across a three-dimensional space. This thermoablation leaves a homogenous resection plane that is markedly dry. The three-dimensional application of electromagnetic energy in a volume of tissue, such as the liver, enables major hepatic arteries and portal veins that are between 10 mm and 20 mm in diameter to be effectively closed.

12. Accordingly, it is my opinion based on the disclosures of Edwards '441, Swanson '760 and Edwards '906 that it would not have been obvious to one of ordinary skill in the art, given the knowledge that heating tissue reduces blood loss, to modify the invention of Edwards '441 as taught by Edwards '906 to use alternate means of heating tissue, and as taught by Swanson '760 to make an incision in the heated tissue in order to reduce blood loss and verify the coagulation depth in the treated tissue. Given these disclosures, one skilled in the art would not have recognized that the three-dimensional application of energy along a planned incision line would result in a bloodless resection of liver tissue.

Under penalty of perjury, I declare that all statements made in the Declaration of my own knowledge are true and that all statement made on information and belief are believed to by true.

Date: November 19, 2007

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